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| 10/528,082 | 03/14/2005 | Joseph D Mosca | | 5825 |

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| EXAMINER | |
|---|---|
| BLANCHARD, DAVID J | |
| ART UNIT | PAPER NUMBER |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/528,082 | MOSCA, JOSEPH D | |
| | Examiner | Art Unit | |
| | David J. Blanchard | 1643 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *27 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-5, 7-8 and 16-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7,8 and 16-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

**DETAILED ACTION**

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 27 April 2009 has been entered.

2. Claims 6 and 9-15 are cancelled.

Claims 1, 3-5, 7-8 and 19 have been amended.

3. Claims 1-5, 7-8 and 16-26 are under consideration.

4. This Office Action contains New Grounds of Rejections

***Objections/Rejections Withdrawn***

5. The rejection of claims 1-7, 16-20 and 23-26 under 35 U.S.C. 102(e) as being anticipated by Hiserodt et al (U.S. 6,277,368 B1, filed 7/24/1997) is withdrawn in view of applicants' arguments and amendments to the claims.

6. The rejection of claims 21-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Nawrocki et al (Cancer treatment Reviews, 25:29-46, 1999) is withdrawn in view of applicants' arguments and amendments to the claims.

*It is noted that the rejection of claim 8 under 35 U.S.C. 112, second paragraph as being indefinite in the recitation "tumor-derived" was withdrawn in the advisory action mailed 2/23/2009.*

***New Grounds of Rejections***

***Claim Rejections - 35 USC § 103***

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. Claims 1-5, 7-8, 16-20 and 23-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hiserodt et al (U.S. 6,277,368 B1, filed 7/24/1997, cited on PTO-892 mailed 11/30/2007) in view of Wagner et al (Intervirology, 39(1)93-103, 1996).

Hiserodt et al teach a method of treating cancer in a subject comprising inducing a cellular immune response involving T cells (i.e., "effector cell immune response") against cancer cells comprising administering tumor cells modified to express a cytokine and optionally altered to express additional cytokines, additional tumor-associated antigens, additional cell-surface molecules, such as adhesion molecules like ICAM-1, histocompatability antigens, or co-stimulation markers like B7-1 or B7-2 and the tumor cells may be autologous or allogeneic, are inactivated and wherein the cytokine-expressing cells are produced using a viral vector such as adenoviral and retroviral vectors (see entire document, particularly cols. 7-10, 15-19, and 21-23). Hiserodt et al do not specifically teach administering a non-infectious, biologically generated virus particle. This deficiency is made up for in the teachings of Wagner et al.

Wagner et al teach non-infectious, non-replicating virus-like particles (VLP) that self-assemble and provide a safe antigen delivery system for inducing a CTL response wherein the VLP can be expressed in host cells, rescued and purified from the cell culture supernatant in good quality and high yields and administration of VLP in subjects stimulates CD8+ CTL in the complete absence of adjuvants (see entire document, particularly pp. 94-95, 98-99, Fig. 4 and Table 1).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to produce a method for treating cancer in a subject comprising producing

non-infectious, non-replicating VLP in the modified autologous or allogenic tumor cells of Hiserodt et al (e.g., expressing one or more tumor antigens in the presence of a co-stimulatory molecule, including B7-1 or B7-2) and administering the isolated/harvested non-infectious, non-replicating VLP for CTL induction and therapeutic benefit in cancer patients.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to produce a method for treating cancer in a subject comprising producing non-infectious, non-replicating VLP in the modified autologous or allogenic tumor cells of Hiserodt et al (e.g., expressing one or more tumor antigens in the presence of a co-stimulatory molecule, including B7-1 or B7-2) and administering the isolated/harvested non-infectious, non-replicating VLP for CTL induction and therapeutic benefit in cancer patients in view of Hiserodt et al and Wagner et al because Hiserodt et al teach a method of treating cancer in a subject comprising inducing a cellular immune response involving T cells (i.e., "effector cell immune response") against cancer cells comprising administering tumor cells modified to express a cytokine and optionally altered to express additional cytokines, additional tumor-associated antigens, additional cell-surface molecules, such as adhesion molecules like ICAM-1, histocompatability antigens, or co-stimulation markers like B7-1 or B7-2 and the tumor cells may be autologous or allogeneic, are inactivated and wherein the cytokine-expressing cells are produced using a viral vector such as adenoviral and retroviral vectors and Wagner et al teach non-infectious, non-replicating virus-like particles (VLP) that self-assemble and provide a safe antigen delivery system for inducing a CTL response wherein the VLP can be expressed in host cells, rescued and purified from the cell culture supernatant in good quality and high yields and administration of VLP in subjects stimulated CD8+ CTL in complete absence of adjuvants. Therefore, one of ordinary skill in the art would have been motivated to modify the method of Hiserodt et al using the VLP for inducing a CTL response in cancer patients, since the VLP are non-infectious, non-replicating and provide a safe antigen delivery system for inducing a CTL response in the complete absence of adjuvant according to Wagner et al. The strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. *In re Sernaker*, 702 F.2d 989, 994-95, 217 USPQ 1, 5-6 (Fed. Cir. 1983). Thus, it

would have been *prima facie* obvious to one skilled in the art at the time the invention was made to produce a method for treating cancer in a subject comprising producing non-infectious, non-replicating VLP in the modified autologous or allogenic tumor cells of Hiserodt et al (e.g., expressing one or more tumor antigens in the presence of a co-stimulatory molecule, including B7-1 or B7-2) and administering the isolated/harvested non-infectious, non-replicating VLP for CTL induction and therapeutic benefit in cancer patients in view of Hiserodt et al and Wagner et al.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

9. Claims 1, 19, 21 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nawrocki et al (Cancer treatment Reviews, 25:29-46, 1999, cited on PTO-892 mailed 8/29/2008) in view of Wagner et al (Intervirology, 39(1)93-103, 1996).

Nawrocki et al teach a method of treating cancer in a subject comprising inducing a cellular immune response involving T cells (i.e., "effector cell immune response") against cancer cells comprising administering autologous non-tumor cells (e.g., dendritic cells, fibroblasts, monocytes) modified using a retroviral, non-viral lipid, or adenoviral gene delivery system to express a tumor antigen, a B7 co-stimulatory molecule and a cytokine (see entire document, particularly abstract, pp. 38-41). Nawrocki et al do not specifically teach administering a non-infectious, biologically generated virus particle. This deficiency is made up for in the teachings of Wagner et al.

Wagner et al have been described supra.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to produce a method for treating cancer in a subject comprising producing non-infectious, non-replicating VLP in the modified non-tumor cells of Nawrocki et al (e.g., expressing a tumor antigen, a B7 co-stimulatory molecule and a cytokine) and administering the isolated/harvested non-infectious, non-replicating VLP for CTL induction and therapeutic benefit in cancer patients.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to produce a method for treating cancer in a subject comprising producing non-infectious, non-replicating VLP in the modified non-tumor cells of Nawrocki et al (e.g., expressing a tumor antigen, a B7 co-stimulatory molecule and a cytokine) and administering the isolated/harvested non-infectious, non-replicating VLP for CTL induction and therapeutic benefit in cancer patients in view of Nawrocki et al and Wagner et al because Nawrocki et al teach a method of treating cancer in a subject comprising inducing a cellular immune response involving T cells (i.e., "effector cell immune response") against cancer cells comprising administering autologous non-tumor cells (e.g., dendritic cells, fibroblasts, monocytes) modified using a retroviral, non-viral lipid, or adenoviral gene delivery system to express a tumor antigen, a B7 co-stimulatory molecule and a cytokine and Wagner et al teach non-infectious, non-replicating virus-like particles (VLP) that self-assemble and provide a safe antigen delivery system for inducing a CTL response wherein the VLP can be expressed in host cells, rescued and purified from the cell culture supernatant in good quality and high yields and administration of VLP in subjects stimulated CD8+ CTL in complete absence of adjuvants. Therefore, one of ordinary skill in the art would have been motivated to modify the method of Nawrocki et al using the VLP for inducing a CTL response in cancer patients, since the VLP are non-infectious, non-replicating and provide a safe antigen delivery system for inducing a CTL response in the complete absence of adjuvant according to Wagner et al. The strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. *In re Sernaker*, 702 F.2d 989, 994-95, 217 USPQ 1, 5-6 (Fed. Cir. 1983). Thus, it would have been *prima facie* obvious to one skilled in the art at the time the invention was made to produce a method for treating cancer in a subject comprising producing non-infectious, non-replicating VLP in the modified non-tumor cells of Nawrocki et al (e.g., expressing a tumor antigen, a B7 co-stimulatory molecule and a cytokine) and administering the isolated/harvested non-infectious, non-replicating VLP for CTL induction and therapeutic benefit in cancer patients in view of Nawrocki et al and Wagner et al.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

10. No claim is allowed.

11. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Roy P. Intervirology, 39(1-2)62-71, 1996.
Roy teaches the use of non-infectious, non-replicating VLPs for vaccine delivery.

Shirmbeck R. et al. Intervirology, 39(1-2):111-119, 1996.
Shirmbeck R. et al teach that VLP without adjuvant as an exogenous antigen preparation that efficiently prime class-I restricted CLT responses.

Greenstone H.L. et al. Proc. Natl. Acad. Sci. USA, 95(4):1800-1805, February 1998.
Greenstone et al teach papillomavirus-like particles that elicit antitumor immunity which is mediated by class-I restricted cytotoxic lymphocytes.

zur Megede J. et al. US Patent 7,211,659, filed 7/5/2002.
zur Megede J. et al teach the production of replication incompetent virus-like particles (VLP) and compositions comprising such wherein the VLP can be used as a matrix for the proper presentation of an antigen entrapped or associated therewith to the immune system and wherein the antigen may include any of the various tumor antigens and wherein the VLP compositions induce a cellular immune response (e.g., induction of a CTL response) (see cols. 15-16, 37-38, 40, 45-47).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The

examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832.

The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/David J. Blanchard/
Primary Examiner, A.U. 1643